



Midazolam

Injection, USP

2 mg per 2 mL | NDC 70860-600-02

25 mg per 5 mL | NDC 70860-601-05

50 mg per 10 mL | NDC 70860-601-10

- **ATHENEX AccuraSEESM PACKAGING AND LABELING**
- **BIG, BOLD AND BRIGHT — TO HELP YOU SEE IT, SAY IT AND PICK IT RIGHT**
- **DIFFERENTIATION IN EVERY LABEL, DESIGNED TO HELP REDUCE MEDICATION ERRORS**



PLEASE SEE FULL PRESCRIBING INFORMATION, INCLUDING BOXED WARNING, FOR MIDAZOLAM INJECTION, USP, ENCLOSED.

THE NEXT GENERATION OF PHARMACY INNOVATION

Midazolam


Injection, USP



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Our proprietary, differentiated and highly-visible label designs can assist pharmacists in accurate medication selection.

With a unique AccuraSEE label design for every Athenex product, we're helping your pharmacy to reduce the risk of medication errors. The idea is simple: "So what you see is exactly what you get."


2 mg
NDC 70860-600-02
2 mg per 2 mL

DESCRIPTION	Glass Vial
CONCENTRATION	1 mg per mL
CLOSURE	13 mm
UNIT OF SALE	25 vials
BAR CODED	Yes



25 mg
NDC 70860-601-05
25 mg per 5 mL

DESCRIPTION	Glass Vial
CONCENTRATION	5 mg per mL
CLOSURE	13 mm
UNIT OF SALE	10 vials
BAR CODED	Yes



50 mg
NDC 70860-601-10
50 mg per 10 mL

DESCRIPTION	Glass Vial
CONCENTRATION	5 mg per mL
CLOSURE	20 mm
UNIT OF SALE	10 vials
BAR CODED	Yes



Midazolam Injection, USP

INDICATIONS AND USAGE

Midazolam Injection, USP indications:

- Intramuscularly or intravenously for preoperative sedation/analgesia/amnesia.
- Intravenously as an agent for sedation/analgesia/amnesia prior to or during diagnostic, therapeutic or endoscopic procedures, such as bronchoscopy, gastroscopy, cystoscopy, coronary angiography, cardiac catheterization, oncology procedures, radiologic procedures, suture of lacerations and other procedures either alone or in combination with other CNS depressants.
- Intravenously for induction of general anesthesia, before administration of other anesthetic agents. With the use of narcotic premedication, induction of anesthesia can be attained within a relatively narrow dose range and in a short period of time. Intravenous midazolam can also be used as a component of intravenous supplementation of nitrous oxide and oxygen (balanced anesthesia).
- Continuous intravenous infusion for sedation of intubated and mechanically ventilated patients as a component of anesthesia or during treatment in a critical care setting.

IMPORTANT SAFETY INFORMATION

WARNINGS

Personnel and Equipment for Monitoring and Resuscitation

Adults and Pediatrics: Intravenous midazolam hydrochloride has been associated with respiratory depression and respiratory arrest, especially when used for sedation in noncritical care settings. In some cases, where this was not recognized promptly and treated effectively, death or hypoxic encephalopathy has resulted. Intravenous midazolam hydrochloride should be used only in hospital or ambulatory care settings, including physicians' and dental offices, that provide for continuous monitoring of respiratory and cardiac function, e.g., pulse oximetry. Immediate availability of resuscitative drugs and age- and size-appropriate equipment for bag/valve/mask ventilation and intubation, and personnel trained in their use and skilled in airway management should be assured (see WARNINGS). For deeply sedated pediatric patients, a dedicated individual, other than the practitioner performing the procedure, should monitor the patient throughout the procedure.

Risks from Concomitant Use with Opioids

Concomitant use of benzodiazepines and opioids may result in profound sedation, respiratory depression, coma, and death. Monitor patients for respiratory depression and sedation (see WARNINGS and PRECAUTIONS, Drug Interactions).

Individualization of Dosage

Midazolam hydrochloride must never be used without individualization of dosage. The initial intravenous dose for sedation in adult patients may be as little as 1 mg, but should not exceed 2.5 mg in a normal healthy adult. Lower doses are necessary for older (over 60 years) or debilitated patients and in patients receiving concomitant narcotics or other central nervous system (CNS) depressants. The initial dose and all subsequent doses should always be titrated slowly administer over at least 2 minutes and allow an additional 2 or more minutes to fully evaluate the sedative effect. The use of the 1 mg/ml formulation or dilution of the 1 mg/ml or 5 mg/ml formulation is recommended to facilitate slower injection. Doses of sedative medications in pediatric patients must be calculated on a mg/kg basis, and initial doses and all subsequent doses should always be titrated slowly. The initial pediatric dose of midazolam for sedation/analgesia/amnesia is age, procedure, and route dependent (see DOSAGE AND ADMINISTRATION for complete dosing in formation).

Neonates: Midazolam should not be administered by rapid injection in the neonatal population. Severe hypotension and seizures have been reported following rapid IV administration, particularly with concomitant use of fentanyl (see DOSAGE AND ADMINISTRATION for complete information).

CONTRAINDICATIONS

- Injectable midazolam hydrochloride is contraindicated in patients with a known hypersensitivity to the drug. Benzodiazepines are contraindicated in patients with acute narrow-angle glaucoma. Benzodiazepines may be used in patients with open-angle glaucoma only if they are receiving appropriate therapy. Measurements of intraocular pressure in patients without eye disease show a moderate lowering following induction with midazolam hydrochloride; patients with glaucoma have not been studied.

- Midazolam hydrochloride multi-dose vial, is not intended for intrathecal or epidural administration, and is contraindicated for use in premature infants, because the formulation contains benzyl alcohol as a preservative.

WARNINGS

- Prior to the intravenous administration of midazolam hydrochloride in any dose, the immediate availability of oxygen, resuscitative drugs, age- and size-appropriate equipment for bag/valve/mask ventilation and intubation, and skilled personnel for the maintenance of a patent airway and support of ventilation should be ensured.
- Patients should be continuously monitored for early signs of hypoventilation, airway obstruction, or apnea with means readily available (e.g., pulse oximetry).
- The immediate availability of specific reversal agents (flumazenil) is highly recommended.
- Because intravenous midazolam can depress respiration, especially when used concomitantly with opioid agonists and other sedatives, it should be titrated slowly when used for sedation/analgesia/amnesia.
- Concomitant use of benzodiazepines, including midazolam, and opioids may result in profound sedation, respiratory depression, coma, and death.
- Serious cardiorespiratory adverse events have occurred after administration of midazolam. These have included respiratory depression, airway obstruction, oxygen desaturation, apnea, respiratory arrest and/or cardiac arrest, sometimes resulting in death or permanent neurologic injury.
- Midazolam hydrochloride must never be used without individualization of dosage particularly when used with other medications capable of producing central nervous system depression.
- Reactions such as agitation, involuntary movements (including tonic/clonic movements and muscle tremor), hyperactivity and combativeness have been reported in both adult and pediatric patients and may be due to inadequate or excessive dosing or improper administration of midazolam hydrochloride; however, consideration should be given to the possibility of cerebral hypoxia or true paradoxical reactions.
- Concomitant use of barbiturates, alcohol or other central nervous system depressants may increase the risk of hypoventilation, airway obstruction, desaturation, or apnea and may contribute to profound and/or prolonged drug effect. Narcotic premedication also depresses the ventilatory response to carbon dioxide stimulation.
- Higher risk adult and pediatric surgical patients, elderly patients, and debilitated adult and pediatric patients require lower dosages, whether or not concomitant sedating medications have been administered.
- Injectable midazolam should not be administered to adult or pediatric patients in shock or coma, or in acute alcohol intoxication with depression of vital signs. Particular care should be exercised in the use of intravenous midazolam in adult or pediatric patients with uncompensated acute illnesses, such as severe fluid or electrolyte disturbances.
- The safety and efficacy of midazolam following non-intravenous and non-intramuscular routes of administration have not been established. Midazolam hydrochloride should only be administered intramuscularly or intravenously. Extravasation should be avoided.
- It is recommended that no patient operate hazardous machinery or a motor vehicle until the effects of the drug, such as drowsiness, have subsided or until 1 full day after anesthesia and surgery, whichever is longer. For pediatric patients, particular care should be taken to assure safe ambulation.
- If this drug is used during pregnancy, the patient should be apprised of the potential hazard to the fetus, and is not recommended for obstetrical use.
- Rapid injection should be avoided in the neonatal population.
- The recommended dosage range of midazolam hydrochloride (multi-dose vial) for preterm and term infants includes benzyl alcohol well below that associated with toxicity; however, the amount of benzyl alcohol at which toxicity may occur is not known. If the patient requires more than the recommended dosages or other medications containing this preservative, the practitioner must consider the daily metabolic load of benzyl alcohol from these combined sources.

- Anesthetic and sedation drugs are a necessary part of the care of children needing surgery, other procedures, or tests that cannot be delayed, and no specific medications have been shown to be safer than any other. Decisions regarding the timing of any elective procedures requiring anesthesia should take into consideration the benefits of the procedure weighed against the potential risks.

PRECAUTIONS

- Intravenous doses of midazolam hydrochloride should be decreased for elderly and for debilitated patients. These patients will also probably take longer to recover completely after midazolam administration for the induction of anesthesia.
- Midazolam does not protect against the increase in intracranial pressure or against the heart rate rise and/or blood pressure rise associated with endotracheal intubation under light general anesthesia.
- Care must be taken to individualize and carefully titrate the dose of midazolam hydrochloride to the patient's underlying medical/surgical conditions, administer to the desired effect being certain to wait an adequate time for peak CNS effects of both midazolam hydrochloride and concomitant medications, and have the personnel and size appropriate equipment and facilities available for monitoring and intervention.
- Exercise caution when midazolam hydrochloride is administered to a nursing woman.

ADVERSE REACTIONS

- The primary adverse events associated with midazolam are related to central nervous system depression, cardiorespiratory events, and possible paradoxical reactions. These include decreased tidal volume/respiratory rate, apnea, dyspnea, shallow respirations, tachypnea, premature ventricular contractions, variations in blood pressure and pulse rate, involuntary movements, hyperactivity and combativeness.
- Other adverse effects include, but are not limited to: headache, injection site reactions (tenderness, pain, redness, induration, phlebitis, warmth, coldness at injection site), hiccups, nausea, vomiting, coughing, drowsiness, retrograde amnesia, hallucination, confusion, blurred vision, diplopia, nystagmus, and allergic/anaphylactoid reactions (hives, rash, pruritus).
- **OVERDOSAGE**
 - Treatment of injectable midazolam overdose is the same as that followed for overdose with other benzodiazepines. Respiration, pulse rate and blood pressure should be monitored and general supportive measures should be employed. Attention should be given to the maintenance of a patent airway and support of ventilation, including administration of oxygen. An intravenous infusion should be started. Should hypotension develop, treatment may include intravenous fluid therapy, repositioning, judicious use of vasopressors appropriate to the clinical situation, if indicated, and other appropriate countermeasures. There is no information as to whether peritoneal dialysis, forced diuresis or hemodialysis are of any value in the treatment of midazolam overdose.
 - Flumazenil, a specific benzodiazepine-receptor antagonist, is indicated for the complete or partial reversal of the sedative effects of benzodiazepines and may be used in situations when an overdose with a benzodiazepine is known or suspected. Prior to the administration of flumazenil, necessary measures should be instituted to secure the airway, assure adequate ventilation, and establish adequate intravenous access. Flumazenil is intended as an adjunct to, not as a substitute for, proper management of benzodiazepine overdose. Patients treated with flumazenil should be monitored for resedation, respiratory depression and other residual benzodiazepine effects for an appropriate period after treatment. Flumazenil will only reverse benzodiazepine-induced effects but will not reverse the effects of other concomitant medications.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch. Or call 1-800-FDA-1088.

Please see full prescribing information for MIDAZOLAM Injection, USP.

